



上海源叶生物科技有限公司
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产品名称:

N-(4-Ethoxyphenyl)-4-(2-methylimidazo-[1,2-a]pyridin-3-yl)thiazol-2-amine

产品别名: **JK184**

生物活性:

Description	JK184 is a potent Hedgehog (Hh) pathway inhibitor with IC ₅₀ of 30 nM in mammalian cells.			
IC₅₀ & Target	IC ₅₀ : 30 nM (Hedgehog)[1]			
In Vitro	JK184 is designed to antagonize Hh signaling by inhibiting glioma (Gli)-dependent transcriptional activity in a dose dependent manner. JK184 significantly inhibits proliferation of HUVECs with IC ₅₀ of 6.3 µg/mL after three days incubation. To evaluate anti-tumor effect of JK184, MTT assay is conducted in Panc-1 and BxPC-3 cells after administration with indicated concentrations of compounds, half maximal inhibitory concentration (IC ₅₀) of JK184 (23.7 ng/mL in anc-1 and 34.3 ng/mL in BxPC-3)[1]. Claudin-low cell lines are more sensitive to JK184 treatment than are MCF10a, MTSV1-7, or HMLE-shGFP and HMLE-pBP cells, and JK184 induced a dose-dependent decrease in glioma-associated oncogene homolog 1 (<i>GLI1</i>) transcript and protein levels in these cells. Treatment with the IC ₅₀ dose of JK184 enhances the proportion of HMLE-shEcad cells that stained with Annexin-V, but are negative for propidium iodide (PI) (P<0.0001, t test)[2].			
In Vivo	JK184 (5 mg/kg, injected intravenously) exhibits good anti-proliferative activity in subcutaneous Panc-1 and BxPC-3 tumor models, and is a good candidate as antitumor drug targeted Hh signaling. However, JK184 has a poor pharmacokinetic profile and bioavailability[1].			
Solvent&Solubility	In Vitro: DMSO : ≥ 50 mg/mL (142.68 mM) * "≥" means soluble, but saturation unknown.			
		Solvent	Mass	Concentration
	Preparing	1 mM	2.8536 mL	14.2678 mL
	Stock Solutions	5 mM	0.5707 mL	2.8536 mL
		10 mM	0.2854 mL	1.4268 mL
	*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80℃, 6 months; -20℃, 1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。 In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline			



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	Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.13 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中, 混合均匀向上述体系中加入 50 μL Tween-80, 混合均匀; 然后继续加入 450 μL 生理盐水定容至 1 mL。 2. 请依序添加每种溶剂: 10% DMSO $\rightarrow$ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.13 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中, 混合均匀。 3. 请依序添加每种溶剂: 10% DMSO $\rightarrow$ 90% corn oil Solubility: ≥ 2.5 mg/mL (7.13 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (7.13 mM, 饱和度未知) 的澄清溶液, 此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。
References	[1]. Zhang N, et al. Biodegradable polymeric micelles encapsulated JK184 suppress tumor growth through inhibiting Hedgehog signaling pathway. <i>Nanoscale</i>. 2015 Feb 14;7(6):2609-24. [2]. Colavito SA, et al. Significance of glioma-associated oncogene homolog 1 (GLI1) expression in claudin-low breast cancer and crosstalk with the nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB) pathway. <i>Breast Cancer Res</i>. 2014 Sep 25;16(5):444.
实验参考:	
Cell Assay	The Shh-LIGHT2 cells are seeded in 96-well plates and grown to confluency. The Shh-LIGHT2 cells are treated with various concentrations of JK184 micelles or free JK184 or micelles in DMEM containing 0.5% CS, 0.1 mg/mL streptomycin, 100 U/mL penicillin, 5% Shh-N conditioned medium obtained from Shh-N-producing HEK293 cells. The treated cells are cultured further for 60 h, and firefly and Renilla luciferase activities are measured using a dual luciferase kit. Proliferation assay or apoptosis evaluation of HUVECs is measured using MTT method or FCM analysis, respectively. HUVECs are treated with a series concentration of free JK184, JK184 micelles, or blank MPEG-PCL micelles for 48 h, respectively. The mean percentage of cell inhibition or apoptosis is calculated[1].
Animal Administration	Mice[1] Five-week-old female athymic (nu/nu) mice are used. BxPC-3 and Panc-1 tumors are established by s.c. injection of 1×10^7 cells. Mice bearing tumors around 100 mm³ are selected and randomized into treatment groups (5 mice per group). Mice are injected intravenously every day for 30 days with 100 μL of NS (control), blank micelles, free JK184 (5 mg/kg body weight), or JK184 micelles (5 mg/kg body weight), respectively. Tumor length and width are determined every 3 days and tumor volume (TV) is calculated using the following formula: $TV = 0.5 \times \text{length} \times \text{width}^2$. At the end of experiment, mice are sacrificed. Solid tumors are removed and processed for immunohistochemical analysis and terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay.
	[1]. Zhang N, et al. Biodegradable polymeric micelles encapsulated JK184 suppress tumor growth



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